REMARKS

The following remarks are submitted in response to the Office Action mailed on September 21, 2006. Claims 24 and 29 have been amended to recite that the first and second amplifiable markers "are the same" and to remove the phrase "amplified by the same amplification agent." Claims 24 and 29 have also been amended to recite "said human antibody." Claim 29 has been amended to recite a heavy or light chain of a human antibody. Claim 25 has been amended to replace the phrase "multi-component protein" with "human antibody."

Support for the claim amendments can be found throughout the specification and claims as originally filed, including at page 22, line 22 to page 24, line 2, page 26, lines 13-31 and Figures 4 and 5. Accordingly, no new matter has been added by way of this amendment. Thus, Claims 24-38 are pending and presented for examination.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects Claims 24-38 under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner alleges that Claims 24 and 29 are not clear because the exact meaning of the phrase "same amplification agent" is allegedly not clear. The Examiner concludes that "amplification agent" refers to agents or chemicals that can be used to initiate the transcription of genes to produce the proteins of interest. Applicants respectfully disagree.

Applicants maintain that the phrase "same amplification agent" is clear from the specification, which teaches that methods for selecting cell lines bearing gene amplifications are known in the art. *See* specification at page 26, lines 21-28 and Figure 4. One of skill in the art would appreciate that culture of cells in the presence of an amplification agent such as methotrexate (MTX) increases the selective pressure for cells bearing multiple copies of an amplification marker such as the dihydrofolate reductase (DHFR) gene. Thus, the phrase "same amplification agent" is clear. Nevertheless, solely in an effort to advance prosecution of the instant claims, Applicants have amended Claims 24 and 29 to remove the phrase "same amplification agent." Accordingly, Applicants respectfully submit that Claims 24 and 29 particularly point out and distinctly claim the subject matter of the invention. Withdrawal of the rejection and allowance of the pending claims is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner rejects Claims 24-38 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Specifically, the Examiner alleges that the specification does not reasonably provide enablement for a method for producing a human antibody wherein the hybrid cell expresses ANY human antibody. Office Action at page 4. The Examiner concludes that the heavy and light chain expression as claimed in the instant claims "have to be of the same antigen specificity" in order to result in an "antigen binding, functional antibody" and that one skilled in the art would allegedly be forced into undue experimentation in order to practice the broadly claimed invention. Office Action at page 6. Applicants respectfully disagree.

Applicants maintain that the specification reasonably provides enablement for the claimed methods. The test for enablement is not merely whether some additional experimentation might be required, but whether the experimentation is "undue experimentation." Applicants note that "[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." (*In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).

In the instant situation, as detailed below, a large amount of guidance has been provided in the specification and figures. Additionally, any additional experimentation would be routine to one of skill in the art, in light of the disclosure in the instant specification. The specification clearly provides a large amount of guidance for one of skill in the art to produce a desired human antibody according to the claimed methods. Further, Example 1 and Figures 4-5 provide clear guidance for one of skill in the art to practice the claimed methods without undue experimentation. Nevertheless, in an effort to increase clarity and advance prosecution of the instant claims, Applicants have amended Claims 24 and 29 to recite a heavy chain polypeptide of "a human antibody" and a light chain polypeptide of "said human antibody." Accordingly, in light of the large amount of guidance in the specification, Applicants respectfully submit that the claims as amended are adequately enabled and request that the rejection be withdrawn and the claims allowed.

Rejection Under 35 U.S.C. § 102(b)

The Examiner rejects Claims 24, 25, 27-32 and 34-38 under 35 U.S.C. § 102(b) as being anticipated by Trill et al. (Current Opinion in Biotechnology 1995, 6: 553-560, hereinafter "Trill") as evidenced by Orlandi et al. (Proc. Natl. Acad. Sci. USA, 86:3833-3837, hereinafter "Orlandi"). Specifically, the Examiner alleges that Trill discloses methods of producing monoclonal antibodies leading to a hybrid cell comprising the heavy and light chain of the desired antibody.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a **single prior art reference**." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987; emphasis added).

Applicants respectfully submit that Trill fails to describe all of the elements of independent Claims 24 or 29 or any of the claims dependent thereon. Trill summarizes issues related to the expression of monoclonal antibodies in COS and CHO cells. The methods taught by Trill allegedly include vectors for expression of antibodies in COS and CHO cells. However, Trill fails to disclose a method of introducing a first polynucleotide into a first mammalian myeloma cell, introducing a second polynucleotide into a second mammalian myeloma cell, culturing the mammalian myeloma cells separately in the presence of an amplification agent, and fusing the cultured cells to form a hybrid cell, as recited in Claims 24 and 29. At best, Trill teaches transfection of vectors separately encoding heavy and light chain polypeptides into the same cell, but Trill does not teach fusion of separately transfected cells to form a hybrid cell. Accordingly, every element and limitation of the claimed invention is not found in Trill as recited in Claims 24 and 29. Applicants respectfully submit that Claims 24 and 29 and their dependent claims are not anticipated under 35 U.S.C. § 102(b). As such, Applicants respectfully request withdrawal of this rejection and allowance of these claims.

Nonstatutory Obviousness-type Double Patenting Rejections

The Examiner rejects instant Claims 24-38 on the judicially created ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 and 5-8 of U.S. Patent No. 6,777,138 in view of Trill as evidenced by Orlandi. The Examiner also rejects

instant Claims 24-38 over Claims 1-4, 6-13 and 15-27 of U.S. Patent No. 6,420,140; over Claims 1-4 and 6-11 of U.S. Patent No. 6,207,418; over Claims 1-4 and 6-11 of U.S. Patent No. 5,916,771, all in view of Trill.

Further, the Examiner provisionally rejects instant Claims 24-38 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 50, 51, 56, 58-65, 67 and 69-74 of copending Application No. 10/155,839 in view of Trill. The Examiner also provisionally rejects instant Claims 24, 25, 29 and 30 over Claims 38-40 of copending Application No. 10/353,844 in view of Trill.

Applicants will consider submitting a terminal disclaimer to overcome the rejection of Claims 24-38 under the judicially created doctrine of obviousness-type double patenting once Claims 24-38 are found to be otherwise allowable.

CONCLUSION

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the new claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully requested to call the undersigned to discuss such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 3/21/07

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AMEND

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